Poster III-15

Analysis of Yeast Competition Experiment for Gene Discovery

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Background
A nearly complete collection of gene-deletion mutants (96% of annotated open reading frames) of the yeast Saccharromyces cerevisiae has been systematically constructed[1,2]. Each deletion is marked with two unique oligonucleotide tags, making it possible to use microarrays to follow the relative abundance and thus the relative fitness of individual strains in a complex mixture.

Aims
Our broad aim is to develop an analytical method to reliably infer individual growth rate of every gene-deletion mutant from a time series of tag microarray data, and to apply this technology to study issues in genome instability by comparing the growth rates of gene-deletion mutants growing under different environments. One specific aim is to identify mutants that show very different growth rates under the two experimental conditions. Such a method may help identifying protein targets of a particular molecule.

Experimental Design
We devised a two-environment, multiple-time-point design. Two collections of gene-deletion mutants are grown under two different environments, e.g. a drug-treated environment and a control environment. Mutant samples are collected from both collections at a series of time points, e.g. 0, 4, 8, and 16 cell generations. DNA of these samples are retrieved, amplified, and hybridized to tag microarrays.

Analytical Method
We developed a strategy to identify mutants that have "significantly" different growth rates under different environments. Here by "significantly" we mean both in the statistical sense and in the scientific sense. The first step was to sort all mutants by a false discovery rate (FDR) in a setting of two-group comparison for the two environments. The mutants with low FDRs were recorded as statistically significant mutants. The second step was to sort the statistically significant mutants by their scientific importance, i.e. by the difference of their estimated growth rates in two environments. For such a purpose we introduced a new statistic, which we named CV, to measure the individual growth rate. With CV we were able to rank the statistically significant mutants by the separation of their inferred growth rates under two different environments.

Conclusion
This work provides an experimental and computational combined approach, which detects mutants with increased or decreased fitness in competition experiments using oligonucleotide tag arrays.

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References

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